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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,932	07/21/2003	Raymond J. Taupier JR.	21402-074CON (CURA-374-CO	6378

7590 09/20/2005

EXAMINER
KOLKER, DANIEL E

ART UNIT	PAPER NUMBER
1649	

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DATE MAILED: 09/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/624,932	TAUPIER ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/3/05, 6/30/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 4-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's remarks and amendments filed 3 February 2005, and sequence listing filed 30 June 2005 have been entered. Applicant has canceled claim 3. Claims 1 – 2 and 4 – 10 are pending and under examination.

2. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejections and Objections

4. The following rejections and objections made in the previous office action are withdrawn:

The objections to the specification are withdrawn in light of applicant's amendments and arguments. .

The objections to the claims are withdrawn in light of applicant's amendments.

The rejections of claim 3 under 35 USC 102. Applicant has cancelled the claim.

New Rejections and Objections

Oath/Declaration

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration, see specifically changes made by inventor Ellerman. See 37 CFR 1.52(c).

Priority

6. 35 U.S.C. § 119(e) states that:

> An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application.

Applicant is advised that the instant application can only receive benefit under 35 U.S.C. § 119(e) from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the now claimed invention. This application is a continuation of 09/918779 and claims benefit of several provisional applications. Provisional application 60/221409, filed 28 July 2000, discloses instantly-disclosed SEQ ID NO:1 and SEQ ID NO:2. However, the provisional application does not constitute an enabling disclosure as it does not teach the artisan how to use the instantly-claimed nucleic acids. Example 1, which appears beginning on p. 131 of the instant specification, discloses the results of TaqMan assays, but there is not disclosure of same in the provisional application. The provisional application does disclose that the instantly-claimed nucleic acid has homology to nucleic acids encoding UNC5H1, but that does not constitute a patentable utility for the reasons set forth below. Priority is granted to the first date that a disclosure identical to the instant disclosure was filed, namely 30 July 2001, the date application 09/918,779 was filed.

Claim Rejections - 35 USC §§ 101 and 112

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1 – 2 and 4 – 10 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to nucleic acids which encode NOV1 or portions thereof. The specification asserts, on the basis of structural similarity to nucleic acids which encode previously known proteins of the UNC-5 family, that the instantly-claimed nucleic acids are useful as diagnostics or therapeutics, or as targets for therapeutics. This is not a specific and substantial patentable utility.

Page 10 of the specification discloses that the instantly-claimed nucleic acid is 89% identical to rat UNC5H1-encoding mRNA. The specification discloses that UNC5H1-like proteins are netrin receptors. There was agreement in the prior art that UNC5 homologs are

netrin-binding proteins (see for example Wang et al. 1999. Journal of Neuroscience 19:4938-4947). However the standard for membership in the UNC5 family is very low. Leonardo et al. (1997. Nature 386:833 – 838) teach that vertebrate homologs of *C. elegans* UNC-5 are only 52% identical to each other and only 28% identical to the protein from the nematode (see p. 835 first column). Applicant has not disclosed a nexus between members of the UNC5 family and any disease or condition. Page 17 of the specification asserts that nucleic acids encoding members of the UNC5H family are useful for treating "patients suffering from neurological and/or other pathologies/disorders". However there is no disclosure of any pathology or disorder that can be treated by the instantly-claimed nucleic acids, nor is there a disclosure of any disease or condition which is characterized by too much or too little of the NOV1 nucleic acid or protein. Clearly the assertion of utility as a homolog of UNC5H would require considerable amounts of research on the part of a skilled artisan. The artisan would first have to identify a disease or condition which is affected by NOV1 and then determine how to use the claimed nucleic acids in order to treat the disease or condition. An invention is said to have substantial utility if it is ready-to-use form and does not require considerable research on the part of the artisan in order to determine how to use it. This is not the case for this asserted utility. Furthermore the asserted utility is not specific, as there is no particular disease or condition which is disclosed to be associated with the nucleic acid or encoded protein.

The specification also asserts that NOV1-encoding nucleic acids are useful in diagnosis of cancers. Examples 1 and 2, beginning on p. 131 of the specification, disclose the results of experiments in which primers amplifying a fragment of SEQ ID NO:1 were used in an RT-PCR assay. This is not a specific and substantial utility. There is no disclosure of whether or not the observed differences are statistically significant or if they are to be expected by random variation. Given the totality of the data presented, many of the differences appear to be within the normal range of variability of the assay. The two columns presented beginning on p. 140 of the specification represent replicates of the experiment (see text on p. 152). In the data reported from ovarian tissue (see p. 142) several cancer samples have only the slightest amount of expression (0.2 or 0.4 or 1.0 as compared to 0.0 for control tissue). Furthermore two tumors appear to have elevated expression (ovarian ca. OVCAR-5 and IGROV-1) but there is very poor repeatability between the two replicates; the first value obtained is almost twice as large as the second value. There is no indication as to whether the artisan should use the maximum value, the minimum value, or the mean as a representative number. Furthermore

there as only one normal sample from ovary was tested the artisan would not be able to determine the level of variability that occurs within a normal, unaffected population and thus could not reasonably determine if the elevated values reported are within the normal range or not. Of the six ovarian cancer samples tested, values above 1.4 were only observed in two. Assaying ovarian cancer samples clearly gives an unreasonable number of false negative results (i.e. expression of NOV1 is low even when cancer is present) and thus the nucleic acid could not reasonably be construed as a diagnostic agent. While the detailed analysis presented above is to the ovarian samples, similar reasoning also applies to samples taken from kidneys (p. 141, bottom half: only two of six samples from cancer show any elevation and even these show up to 100% inter-experiment variation), lung (p. 143, middle: inter-experiment variation is over 3-fold for normal tissue and there is considerable overlap between cancer and normal values), and breast (inter-experiment variation is at least two-fold, many cancerous tissues have very low levels of NOV1 expression). Thus the specification fails to provide evidence that the nucleic acid can be used in its current form to diagnose any disease.

Furthermore, while the claims are drawn to SEQ ID NO:1 or specific fragments thereof, or to nucleic acids which encode SEQ ID NO:2 or specific fragments thereof, the experiments reported in Examples 1 and 2 of the specification do not use any of the claimed nucleic acids. Table AA on p. 140 of the specification indicates that the region amplified in those experiments was the region between nucleotides 2184 and 2247 of SEQ ID NO:1. While the specification discloses that SEQ ID NO:1 is a nucleic acid that encoded the polypeptide SEQ ID NO:2, the specification does not provide evidence of a patentable utility for SEQ ID NO:2. The genetic code, which specifies how nucleic acids are translated to proteins, is degenerate. This means that a single protein can be encoded by multiple nucleic acid codons (see Alberts et al., Molecular Biology of the Cell, p. 232). While applicant has provided asserted a utility for a fragment of SEQ ID NO:1, there is not a utility for nucleic acids which encode the protein SEQ ID NO:2 as this includes many nucleic acids which are not identical to SEQ ID NO:1 and differ in the region used in the TaqMan assay reported in Example 2.

Thus the artisan would have to engage in considerable additional research to know how to use the invention of claims 1 – 2 and 4 – 10, therefore the asserted utilities as either a diagnostic or a therapeutic are not specific and substantial.

9. Claims 1 – 2 and 4 10 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial

asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1, 2, 4 – 6 and 10 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20, 21, and 25 of copending Application No. 10/453372. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of claim 20 of the '372 application includes instantly-claimed SEQ ID NO:1. Claim 20 of the '372 application is drawn to isolated nucleic acids having SEQ ID NO:2n – 1, where n is an integer from 1 - 606. SEQ ID NO:513 of the '372 application is identical to instantly-claimed SEQ ID NO:1. Thus if n = 257 claims 20, 21, and 25 of the '372 application read on pending claims 1, 2, 4 – 6 and 10.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel E. Kolker, Ph.D.
September 1, 2005

SHARON TURNER, PH.D.
PRIMARY EXAMINER
9-15-05